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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/627,649

07/28/2003

Lena Edelman

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4213

22852

7590

04/10/2008

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EXAMINER

HORNING, MICHELLE S

ART UNIT

PAPER NUMBER

1648

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/627,649	<b>Applicant(s)</b> EDELMAN ET AL.	
	<b>Examiner</b> MICHELLE HORNING	<b>Art Unit</b> 1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 10 January 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 35, 46, 59, 60, 64-66 and 68-90 is/are pending in the application.
- 4a) Of the above claim(s) 35, 59, 60, 64-68 and 85-90 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 46, 69-84 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

This office action is responsive to communication filed 1/10/2008. The status of the claims is as follows: claims 46 and 69-84 are under current examination.

#### ***Claim Rejections - 35 USC § 103-NECESSITATED BY CLAIM AMENDMENTS***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 46 and 69-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Aqeilan et al (1999), Bredesen, Kim et al (1997), Huang et al, Sela and Zisman (1997) and US Patent # 6342221 (hereinafter as "Thorpe").**

Briefly, the prior art was applied as discussed below.

1. The amino acid sequence set forth by SEQ ID NO: 239 is disclosed by the prior art. The peptide is known to inhibit the anti-apoptotic function of Bcl-2. Thus, the cited reference by Huang et al provides both the structure and the function of the claimed sequence. Further, this reference provides a method of intracellular targeting of Bcl-2 using peptide conjugates.

2. The crucial motif necessary for the functional translocation mediated by the tat protein has been well-described by Kim et al. The last office action clearly states that this motif is found in the sequence of SEQ ID NO: 269. Also noted is that the instant specification fails to provide any novel function of the peptide set forth in SEQ ID NO: 269 in addition to the already well-described motif characterized by the teachings of Kim et al.

3. Bredesen teaches a peptide which consists of the sequence set forth by SEQ ID NO: 269. In addition, the author teaches linking this peptide to a number of other peptides and demonstrates that this peptide does not alter the function of the peptide attached to the peptide set forth by SEQ ID NO: 269.

4. Peptides comprising D-amino acids resist enzymatic degradation as taught by Sela and Zisman.

5. The newly applied reference by Thorpe provides the following recitations with respect to a peptide linker comprising a cleavable site within a fusion protein: "it is contemplated that biologically-releasable bonds and selectively-cleavable sequences will be particularly useful in this regard, with the bond or sequence only being cleaved or otherwise

modified upon localization within the tumor environment and exposure to particular enzymes or other bioactive molecules" (paragraph 237). This paragraph further discusses prevention of potential hindering of the peptide's functional properties and how this may be alleviated by the selectively-cleavable sequences. The author provides examples in the following recitation:

"Exemplary forms of such peptide linkers are those that are cleaved by urokinase, plasmin, thrombin, Factor IXa, Factor Xa, or a metalloproteinase, such as collagenase, gelatinase or stromelysin" (see paragraph 235).

6. Lastly, the teachings of Aqeilan et al provide a functional chimeric protein in which the human Bax protein may be used to induce apoptosis. Thus, apoptosis inducing chimeric proteins are well known in the art and have been demonstrated to be functional.

In conclusion, it would have been obvious to one of ordinary skill in the art to modify the methods taught by the above references in order to make a bifunctional, chimeric molecule comprising D-amino acids that enters cells and induces apoptosis. One would have been motivated to do so, as suggested by Aqeilan et al (1999), because killing cells via the apoptotic pathway minimizes any tissue damage or systemic response (see Discussion). There would have been a reasonable expectation of success due to the taught successes of the applied prior art, notably by Aqeilan et al. Further, both peptides (SEQ ID NO: 239 and 269) are well described in the art, both

functionally and structurally. Thus, the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Applicant's arguments have been considered but not found to be persuasive. In response, Applicant has questioned the applied motivation to combine the prior art references. It is not clear to the Examiner how this is unclear. The peptide of SEQ ID NO: 239 is known to induce apoptosis. Killing cells via the apoptotic pathway minimizes any tissue damage or systemic response as taught by Aqelian et al. Separately, the Applicant argues that the claims are drawn to a Targ-Tox, wherein the Tox and Targ *consist* of the peptide. Huang et al discloses SEQ ID NO: 239 and Bredeisen provides SEQ ID NO: 269. Tat translocates and proapoptotic peptides induce apoptosis. Killing cells via the apoptotic pathway minimizes any tissue damage or systemic response. This rejection is maintained.

### ***Conclusion***

NO CLAIM IS ALLOWED.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the

Art Unit: 1648

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELLE HORNING whose telephone number is (571)272-9036. The examiner can normally be reached on Monday-Friday 8:00-5:00 EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michelle Horning/

Application/Control Number: 10/627,649

Page 7

Art Unit: 1648

Examiner, Art Unit 1648

/Bruce Campell/

Supervisory Patent Examiner, Art Unit 1648